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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/014,785	12/14/2001	Chensheng Li	041457-0635	1693

22428 7590 10/03/2003

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EXAMINER	
GHALI, ISIS A D	

ART UNIT	PAPER NUMBER
1615	

DATE MAILED: 10/03/2003

9

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/014,785	LI ET AL.	
	Examiner	Art Unit	
	Isis Ghali	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 July 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-15,18-32 and 35* is/are pending in the application.

4a) Of the above claim(s) *18-32 and 35* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-15* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *5, 6* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *page 2367 from PDR* .

DETAILED ACTION

The receipt is acknowledged of applicants' election and request for extension of time, both filed 07/21/2003.

Claims 16, 17, 33 and 34 have been canceled.

Response to Election/Restrictions

1. Applicant's election with traverse of Group I claims 1-15 in Paper No. 8 is acknowledged. The traversal is on the ground(s) that there can be no serious burden on the examiner in searching Groups I and II together because the claims of both groups are classified in the same class and subclass and the search of the claims of Group I will encompass a search of the claims of Group II. This is not found persuasive because Group I requires the administration of the drug itself while Group II requires the administration of the prodrug that is lipophilic. The summary of the present invention, page 4 [0007], identifies two distinct objectives and represents two different processes: one uses composition comprising the prodrug enalapril ethyl ester, and second uses the drug enalaprilat. The specification page 7 [0018], discloses that the present inventors have unexpectedly discovered that the flux of the polar drug enalaprilat in its water soluble form through the skin is negligible, while that of the lipophilic enalapril ethyl ester prodrug is significantly greater.

Group I is directed to non-prodrug that has the carboxylic acid groups are cleaved. Group II directed to the prodrug that has the carboxylic acid group not cleaved, see chemical structure at page 5 [0007].

The restriction between two processes that have two distinct mechanisms is proper, even when the inventions are classified in the same area.

Applicants are entitled to one invention per patent. The use of a prodrug versus the use of a drug is patentably distinctive, especially since:

a) The prodrug has different properties.

b) The mechanism of action is not the same.

c) Different and distinct drugs are used.

See the attached paper, from PDR, that shows benazepril hydrochloride, one of the claimed drugs in Group II, where the active metabolite of benazepril is converted to benazeprilat by hepatic cleavage of the ester groups.

For group I, the two carboxylic groups have been cleaved, see page 5 of specification [0007].

Species election is moot in view of applicants' amendment that canceled the claims that contain the species.

The requirement is still deemed proper and is therefore made FINAL.

2. Claims 18-32, and 35 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected Group II, there being no allowable

generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 8.

Claims 1-15 are included in the prosecution.

Claim Rejections - 35 USC § 102

3. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

4. Claim 9 is rejected under 35 U.S.C. 102(e) as being anticipated by US '6,387,984 ('984).

US '894 disclosed a composition and method of achieving a therapeutic effects including the treatment of heart failure or hypertension (abstract). The method comprises administration of a composition comprising ethyl ester of analapril in pharmaceutically acceptable carrier (col.12 lines 11-13; col.13, lines 30-37). The method of administration included the transdermal route (col.13, line 16; col.14, line 9).

Claim Rejections - 35 USC § 103

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

6. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

7. Claims 1-15 are rejected under 35 U.S.C. 103(a) as being unpatentable over US 6,387,894 ('894) in view of US 2002/0004065 ('065).

US '894 teaches a composition and method of achieving a therapeutic effects including the treatment of heart failure or hypertension (abstract). The method comprises administration of a composition comprising ethyl ester of analapril in

pharmaceutically acceptable carrier (col.12 lines 11-13; col.13, lines 30-37). The method of administration included the transdermal route (col.13, line 16; col.14, line 9).

US '894 does not teach that the flux rate of enalapril ethyl ester is greater than the enalapril maleate, or that the carrier comprising pressure sensitive adhesives and permeation enhancers.

It is expected by one having ordinary skill in the art to obtain the same flux rate from the same compound administered by the same route, absent evidence to the contrary. The claimed flux rates do not impart patentability to the claims.

US '065 teaches a composition method for transdermal drug delivery of active agent up to a period of seven days or more at substantially zero-order release rate providing a release rate regulating effect on the active agent (abstract). The active agents include enalapril (page 10, 0161). The composition comprising polysiloxane and polyacrylate as pressure sensitive adhesives, and dipropylene glycol and oleyl alcohol as permeation enhancers (Table I on page 5).

Thus, it would have been obvious to one having ordinary skill in the art at he time of the invention to provide a method and composition for transdermal administration of enalapril ethyl ester as disclosed by US '894, and provide the drug in an adhesive carrier comprising permeation enhancer as disclosed by US '065, motivated by the teaching of US '065 that the disclosed composition and method deliver the active agent up to a period of seven days or more at substantially zero-order release rate providing a release rate regulating effect on the active agent, with reasonable expectation of having

a transdermal delivery method and composition that provide a high flux rate of enalapril ethyl ester to be delivered to patient in need with success.

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Isis Ghali whose telephone number is (703) 305-4048. The examiner can normally be reached on Monday through Thursday from 7:00 AM to 5:30 PM, Eastern Time.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thurman Page, can be reached on (703) 308-2927. The fax phone number for the organization where this application or proceeding is assigned is (703) 305-3592.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 305-1235.

Isis Ghali
Examiner
Art Unit 1615

Isis Ghali

ISIS GHALI
PATENT EXAMINER